Commentary to Feature Review: Searching for the Origins of Schizophrenia
Review by: Rue L. Cromwell
Psychological Science, Vol. 4, No. 5 (Sep., 1993), pp. 276-279
Published by: Sage Publications, Inc. on behalf of the Association for Psychological Science
Stable URL: http://www.jstor.org/stable/40063046
Accessed: 15/06/2014 11:42

Your use of the JSTOR archive indicates your acceptance of the Terms & Conditions of Use, available at
http://www.jstor.org/page/info/about/policies/terms.jsp

JSTOR is a not-for-profit service that helps scholars, researchers, and students discover, use, and build upon a wide range of content in a trusted digital archive. We use information technology and tools to increase productivity and facilitate new forms of scholarship. For more information about JSTOR, please contact support@jstor.org.

Sage Publications, Inc. and *Association for Psychological Science* are collaborating with JSTOR to digitize, preserve and extend access to *Psychological Science.*

http://www.jstor.org

This content downloaded from 62.122.79.31 on Sun, 15 Jun 2014 11:42:41 AM
All use subject to JSTOR Terms and Conditions

1979), sensory gating (Siegel, Waldo, Mizner, Adler, & Freedman, 1984), and span of apprehension (Wagener, Hogarty, Goldstein, Asarnow, & Browne, 1986). The point is that our model can integrate diverse findings of abnormality in schizophrenics and their relatives, and can in principle explain such findings by a relatively simple genetic mechanism. Such a model is eminently falsifiable, is quite extensible, and (not unimportant) also offers a central role for psychologists in the exploration of the genetics of schizophrenia.

REFERENCES

Clementz, B.A., Grove, W.M., Iacono, W.G., & Sweeney, J.A. (1992). Smooth-pursuit eye movement dysfunction and liability for schizophrenia: Implications for genetic modeling. *Journal of Abnormal Psychology, 101,* 117–129.

DeAmicus, L.A., & Cromwell, R.L. (1979). Reaction time crossover in process schizophrenic patients, their relatives, and control subjects. *Journal of Nervous and Mental Disease, 167,* 593–600.

Faraone, S.V., & Tsuang, M.T. (1985). Quantitative models of the genetic transmission of schizophrenia. *Psychological Bulletin, 98,* 41–66.

Grove, W.M., Clementz, B.A., Iacono, W.G., & Katsanis, J. (1992). Smooth pursuit ocular motor dysfunction in schizophrenia: Evidence for a major gene. *American Journal of Psychiatry, 149,* 1362–1368.

Grove, W.M., Lebow, B.S., Clementz, B.A., Cerri, A., Medus, C., & Iacono, W.G. (1991). Familial prevalence and co-aggregation of schizotypy indicators: A multi-trait family study. *Journal of Abnormal Psychology, 100,* 115–121.

Iacono, W.G., & Clementz, B.A. (1993). A strategy for elucidating genetic influences on complex psychopathological syndromes (with special reference to ocular motor functioning and schizophrenia). In L.J. Chapman, J.P. Chapman, & D. Fowles (Eds.), *Progress in experimental personality and psychopathology research: Vol. 16* (pp. 11–65). New York: Springer.

Iacono, W.G., Moreau, M., Beiser, M., Fleming, J.A.E., & Lin, T.-Y. (1992). Smooth-pursuit eye tracking in first-episode psychotic patients and their relatives. *Journal of Abnormal Psychology, 101,* 104–116.

Katsanis, J., & Iacono, W.G. (1991). Clinical, neuropsychological, and brain structural correlates of smooth-pursuit eye tracking performance in chronic schizophrenia. *Journal of Abnormal Psychology, 100,* 526–534.

Matthysse, S., Holzman, P.S., & Lange, K. (1986). The genetic transmission of schizophrenia: Application of Mendelian latent structure analysis to eye tracking dysfunctions in schizophrenia and affective disorder. *Journal of Psychiatric Research, 20,* 57–76.

Meehl, P.E. (1962). Schizotaxia, schizotypy, schizophrenia. *American Psychologist, 17,* 827–838.

Siegel, C., Waldo, M., Mizner, G., Adler, L.E., & Freedman, R. (1984). Deficits in sensory gating in schizophrenic patients and their relatives. *Archives of General Psychiatry, 41,* 607–612.

Su, Y., Burke, J., O'Neill, F.A., Murphy, B., Nie, L., Kipps, B., Bray, J., Shinkwin, R., Nuallin, M.N., MacLean, C.J., Walsh, D., Diehl, S.R., & Kendler, K.S. (1993). Exclusion of linkage between schizophrenia and the D_2 dopamine receptor gene region of chromosome 11q in 112 Irish multiplex families. *Archives of General Psychiatry, 50,* 205–211.

Wagener, D.K., Hogarty, G.E., Goldstein, M.J., Asarnow, R.F., & Browne, A. (1986). Information processing and communication deviance in schizophrenic patients and their mothers. *Psychiatry Research, 18,* 365–377.

Commentary to Feature Review

SEARCHING FOR THE ORIGINS OF SCHIZOPHRENIA

Rue L. Cromwell

University of Kansas

In this Commentary, I deal with selected issues concerning the origins of schizophrenia, filling out the picture presented by the books under review. Included are comments on definition, older and enduring notions about origins, some more recent notions, and, finally, some potentially useful but not fully exploited notions. George Bernard Shaw (1907, pp. 140–141) suggested that people are immediately willing to give up an obsolete tool such as a wooden plow or hand-cranked car, but they are most unwilling to give up an obsolete idea or concept. While the concept of schizophrenia does not appear ready to be replaced, some notions about its origins appear worthy of examination.

DEFINITION

Schizophrenia refers to a set of behavioral dimensions that concur in deviant form frequently enough to be referred to as a syndrome or disorder. Yet M. Bleuler has recently reminded us that his father, who coined the term (E. Bleuler, 1911/1950), viewed it as a group of disorders (see Cromwell, in press-a). Most investigators assume a unity, although some suggest plurality (subtyping). Final evidence has not yet been obtained for either view. From a heuristic standpoint, a plural view would indicate that differential defining criteria would point to differential treatment implications, course, and prognosis.

Another issue in the definition of schizophrenia has been the shift away from the relatively existential definition: Bleuler's (1911/1950) definition in terms of associative disturbance, affective splitting, ambivalence, and autistic meaning assignments and the definition of prior editions of the *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association, APA, 1952, 1965) in terms of disturbance in reality relationships. In place of the existential definitions has come the use of operational criteria (APA, 1980, 1987). With this shift, schizophrenia has become objectively defined pri-

Address correspondence to Rue L. Cromwell, Department of Psychology, University of Kansas, Lawrence, KS 66045.

This content downloaded from 62.122.79.31 on Sun, 15 Jun 2014 11:42:41 AM
All use subject to JSTOR Terms and Conditions

marily in terms of delusions, hallucinations, thought disorder, and their relevant time parameters. It is widely acknowledged that this shift has achieved stronger interobserver reliability, but the utility of the operational criteria for either genetic-etiologic depiction or clinical decision making and prediction remains controversial (Cromwell, 1982).

ORIGINS: FAMILIAL AND STRESS

Older and enduring notions about origins are that schizophrenia runs in (some) families and may be contributed to, or reactivated by, stress. That it runs in families is attested to by numerous concordance studies (e.g., one affected parent–offspring, 13%; sibling–sibling, 9% to 17%; dizygotic twins, 17%; monozygotic twins, 48%; see Gottesman, 1991, p. 96). That it runs (observably) only in some families follows from the fact that 89% of diagnosed schizophrenics have no known relative who is schizophrenic.

Whether stress contributes to onset is a question hampered by inadequate definitions and lack of study. Of potential stressors that might be important, growing up in a family with a schizophrenic parent or other family member appears inconsequential (Gottesman & Bertelsen, 1989). Whether stress may be a sole contributor (save that it must be inflicted upon a genetically endowed organism) is an age-old question. Gottesman and Bertelsen (reported in Gottesman, 1991, p. 102) found that Danish patients diagnosed with reactive or psychogenic psychoses (precipitated clearly by stressful events) had offspring at no greater risk for psychosis than the general population. That stress may reactivate an episode appears well documented in the studies of expressed emotion (Miklowitz & Goldstein, in press).

See Gottesman (1991) for what is perhaps the most user- and mental health consumer-friendly book ever written on familial origins. See Walker (1991) for a penetrating view of how familial and stress factors come together in the life-course development of schizophrenia.

The Genetic Hypotheses

The obstacles in advancing these familial data to the affirmation of a clear genetic factor are many. No clear Mendelian pattern of transmission from generation to generation exists for schizophrenia. To explain the lack of expected instances across generations, the concept of incomplete penetrance is widely invoked. When psychometricians encounter such failures in prediction, they often call them false negatives and search for measures and variables which would improve their predictions. It is possible that the term penetrance has become reified in a way which obstructs this type of inquiry.

Another obstacle is that no specificity of genetic transmission has been identified. No chromosomal, gene, or DNA-segmental locus has been successfully associated with schizophrenia. Linkage analyses have made it possible to identify the presence or absence of a trait occurring across generations in correspondence with the presence or absence of a gene or DNA segment already of known chromosomal origin and location, providing that these two factors are close enough to each other on the same chromosome so as not to get separated in the generational transmission. For schizophrenia (or spectrum disorders thereof) as a trait, no such linkage study has yet proven replicable (e.g., Wang, Black, Andreasen, & Crowe, 1993).

A third, and related, obstacle has been the lack of agreement about how many genes are transmitted in familial schizophrenia. Could there be several genes that increase vulnerability but are not specific to schizophrenia? Could there be several genes at least some of which have specificity to schizophrenia (a typical polygenic model)? Could there be one single and crucial schizophrenia gene (a monogenic model)? Or could there be a very limited number of crucial genes (an oligogenic model)? No evidence yet available conclusively argues for one or the other of these models.

Recent thinking and data have leaned toward the oligogenic hypothesis. One major piece of evidence against additive polygenic and also monogenic models is that the drop-off in incidence of schizophrenia does not parallel the drop-off in shared inheritance with a proband. From monozygotic twins to dizygotic twins (and siblings) to grandchildren (or other second-degree relatives), the drop-off in shared inheritance is 50% with each step: 100% to 50% to 25%. The drop-off in the incidence of schizophrenia is greater: 48% to 9–17% to 4–6%. In a diffuse additive polygenic model, one could expect a successive 50% drop-off. However, an observation compatible with the polygenic notion is that the severity of schizophrenia in an index case is correlated with the number of relatives who have been diagnosed with schizophrenia. This observation is usually (but not necessarily) interpreted to indicate that the number of polygenic factors inherited accounts for both the clinical severity and the number of cases in the family.

An argument against a monogenic model comes from observations (De Amicis, Wagstaff, & Cromwell, 1986; Heston, 1966; McCarthy, 1993; McNeil, 1971) that the nonaffected relatives of schizophrenics have a higher extent of creativity or educational-occupational achievement compared with normal control subjects. Such a finding requires at least two factors. For example, one factor may involve a heightened sensitivity, and a second factor may define the direction (disintegration or elevated functioning; Cromwell, in press-b; Kendler & Eaves,

This content downloaded from 62.122.79.31 on Sun, 15 Jun 2014 11:42:41 AM
All use subject to JSTOR Terms and Conditions

1986) this sensitivity will take. The second factor may be genetic or environmental; thus, the argument against a monogenetic model is not conclusive. Incidentally, such evidence of high functioning in the normal, healthy relatives of people with schizophrenia presents a serious challenge to notions that schizophrenia is a faulty scientific construct based solely upon unwanted behavior (Sarbin, 1991).

Potentially one of the most important studies of the origins of schizophrenia in recent years has been by Gottesman and Bertelsen (1989), who investigated the offspring of monozygotic and dizygotic schizophrenic twins and their discordant (unaffected) co-twins. Offspring of affected monozygotic twins had a 16.8% risk for schizophrenia, and the offspring of their normal co-twins had 17.4% risk. By contrast, offspring of dizygotic schizophrenic twins had a 17.4% risk, but the offspring of their normal co-twins had only 2.1% risk. Attention is usually placed on the high incidence of schizophrenia among the offspring of the normal monozygotic co-twins, thus supporting the idea of a genetic transmission and discouraging the notion that growing up with a schizophrenic parent is crucial in interpreting twin data. However, the more important finding may be the precipitous drop-off in incidence among the offspring of the normal dizygotic co-twins (i.e., only 2.1%). Such a drop is not compatible with either an additive polygenic or a monogenic model. Instead, the drop-off suggests a configurational (interactive) oligogenic model in which all factors must be in place to produce the condition.

Unexploited Avenues of Genetic Inquiry

Trying to study schizophrenia genetics with clinical diagnosis as the phenotype may be like studying the genetics of color blindness through familial tendencies to run traffic lights. Numerous genetic and environmental factors may be involved. It may be better to move to the laboratory, with controlled testing of contributory factors. Straube and Oades (1992) refer to these factors as "experimental symptoms." In brief, the unwieldy clinical phenotype calls for the search for the phenotype(s) more closely associated with the genetic variance. It is here that the science of psychology may need to provide leadership in elucidating the behavioral mechanisms with clear neuroscience and genetics correlates.

To adopt the laboratory approach—that is, to study schizophrenia-related variants (SRVs)—raises other questions. First, on the one hand, attention/information processing (A/IP) variables may be looked upon as a subclass of etiologies (e.g., Gottesman, 1991). On the other hand, the totality of cognitive brain functioning, including schizophrenia, may be conceptualized in an A/IP framework. Second, on the one hand, the SRVs may be viewed as pleiotropic; that is, the genotype (or latent trait) may be viewed as alternatively expressed by the clinical disorder or the SRVs (Holzman, Kringlen, & Matthysse, 1988). On the other hand, the SRVs may be viewed as preceding the onset of the clinical condition and being closer to the relevant genetic variance (Cromwell, in press-b). The impetus for the latter view comes from findings (e.g., Cornblatt & Erlenmeyer-Kimling, 1983) that A/IP measures (e.g., vigilance) not only preceded but predicted later onset of psychiatric disturbance.

Pursuing hypotheses of oligogenic models in particular raises a number of questions. First, will it be necessary to use latent structure analyses in order to combine and remove method variance from these A/IP variables (Spohn & Coyne, 1989)? Second, does a configurational (interactive, multiplicative) or an additive model best fit the data? An additive model implies that a monotonic increase in probability of schizophrenia occurs with an increasing number of relevant genes. A configurational model implies that the exact genes, small in number, must be in place before schizophrenia is manifested. The latter model would explain the precipitous drop-off in risk for schizophrenia in the Gottesman and Bertelsen (1989) study described above. Such a model would also explain why (a) some relatives, who may inherit only part of the configuration, are deviantly positive in creativity or other functioning; (b) most relatives appear at zero risk; and (c) other relatives appear more vulnerable than the actuarial figures described above indicate. Oligogenic hypotheses point to a need for commingling (admixture) analyses of distributions of first-degree relatives.

Unexploited Avenues of Environmental Inquiry

Beyond the diagnostic boundaries of schizophrenia, there has been increasing attention among researchers to the fact that psychological trauma (e.g., rape, combat, massacre, natural disaster) affects an individual's ability to develop and operate upon the contents of memory (Foa & Riggs, 1993; Sewell, 1991). In effect, people with trauma are found unable to retrieve "a good narrative" of what happened to them, to relate or compare the trauma with other negative or positive events in life. Research has linked dissociation (Chu & Dill, 1990) and Schneiderian first-rank symptoms (Kluft, 1987) to the effects of these traumas. Aspects of these dissociation and Schneiderian items appear similar to aspects of schizotypy and schizophrenia spectrum measures (Chapman, Chapman, & Raulin, 1978; Erkblad & Chapman, 1983; Kendler, 1988). Although the disorders ordinarily associated with trauma (posttraumatic stress disorder, or PTSD; multiple personality disorder) are not considered psychotic, they could be viewed as a variation of thought disorder. Is it too hazardous to speculate that PTSD and other trauma

This content downloaded from 62.122.79.31 on Sun, 15 Jun 2014 11:42:41 AM
All use subject to JSTOR Terms and Conditions

effects manifest themselves in individuals who have not inherited the genetic variance related to schizophrenia? Is it not also possible that these acquired cognitive deficits in response to psychological trauma help complete the schizophrenia syndrome in people who have indeed inherited the genotype(s)? The recent work on hierarchical classification of the conceptual structure of people with schizophrenia is of particular note (Gara, Rosenberg, & Mueller, 1989). If the trauma effects on cognitive operations may be viewed in this way, more research is needed on cognitive functioning which cuts across diagnostic boundaries.

REFERENCES

American Psychiatric Association. (1952). *Diagnostic and statistical manual for mental disorders* (1st ed.). Washington, DC: Author.

American Psychiatric Association. (1965). *Diagnostic and statistical manual for mental disorders* (2nd ed.). Washington, DC: Author.

American Psychiatric Association. (1980). *Diagnostic and statistical manual for mental disorders* (3rd ed.). Washington, DC: Author.

American Psychiatric Association. (1987). *Diagnostic and statistical manual for mental disorders* (3rd ed., rev.). Washington, DC: Author.

Bleuler E. (1950). *Dementia praecox or the group of schizophrenias* (J. Zinkin, Trans.). New York: International Universities Press. (Original work published 1911)

Chapman, L.J., Chapman, J.P., & Raulin, M.L. (1978). Body-image aberration in schizophrenia. *Journal of Abnormal Psychology, 87,* 399–407.

Chu, J.A., & Dill, D.L. (1990). Dissociative symptoms in relation to childhood physical and sexual abuse. *American Journal of Psychiatry, 147,* 887–892.

Cornblatt, B., & Erlenmeyer-Kimling, L. (1983). Early attentional predictors of adolescent behavioral disturbances in children at risk for schizophrenia. In N. Watt, J. Anthony, L.C. Wynne, & J. Rolff (Eds.), *Children at risk for schizophrenia: A longitudinal perspective* (pp. 198–211). New York: Cambridge University Press.

Cromwell, R.L. (1982). Eight decades focus on symptom classification is enough: A discussion. In M.J. Goldstein (Ed.), *Preventive intervention in psychopathology: Are we ready?* (pp. 114–125). Washington, DC: U.S. Government Printing Office.

Cromwell, R.L. (in press-a). Heritage of the schizophrenia concept. In R.L. Cromwell & C.R. Snyder (Eds.), *Schizophrenia: Origins, processes, treatment, and outcome*. New York: Oxford University Press.

Cromwell, R.L. (in press-b). Schizophrenia research: Things to do before the geneticist arrives. In R.L. Cromwell & C.R. Snyder (Eds.), *Schizophrenia: Origins, processes, treatment, and outcome*. New York: Oxford University Press.

De Amicis, D.A., Wagstaff, D., & Cromwell, R.L. (1986). Reaction time crossover as a marker of schizophrenia and of higher functioning. *Journal of Nervous and Mental Disease, 174,* 177–179.

Erkblad, M., & Chapman, L.J. (1983). *Magical Ideation Scale*. Unpublished manuscript, University of Wisconsin, Madison.

Foa, E.B., & Riggs, D.S. (1993). Posttraumatic stress disorder and rape. *Review of Psychiatry, 12,* 273–303.

Gara, M.A., Rosenberg, S., & Mueller, D.R. (1989). The perception of self and other in schizophrenia. *International Journal of Personal Construct Psychology, 2,* 253–270.

Gottesman, I.I. (1991). *Schizophrenia genesis: The origins of madness*. New York: W.H. Freeman.

Gottesman, I.I., & Bertelsen, A. (1989). Confirming unexpressed genotypes for schizophrenia: Risks in the offspring of Fischer's Danish identical and fraternal discordant twins. *Archives of General Psychiatry, 46,* 867–872.

Heston, L.L. (1966). Psychiatric disorders in foster home reared children of schizophrenic mothers. *British Journal of Psychiatry, 112,* 819–825.

Holzman, P.S., Kringlen, E., & Matthysse, S. (1988). A single dominant gene can account for eye tracking dysfunction and schizophrenia in offspring of discordant twins. *Archives of General Psychiatry, 45,* 641–650.

Kendler, K.S. (1988). *Structured interview for schizotypy*. Unpublished manuscript, Medical College of Virginia, Richmond.

Kendler, K.S., & Eaves, L.J. (1986). Models for the joint effect of genotype and environment on liability to psychiatric illness. *American Journal of Psychiatry 143,* 279–289.

Kluft, R.P. (1987). First-rank symptoms as a diagnostic clue to multiple personality disorder. *American Journal of Psychiatry, 144,* 293–298.

McCarthy, M. (1993). *Reaction time crossover, creativity, and achievement among the relatives of schizophrenic patients*. Unpublished master's thesis, University of Kansas, Lawrence.

McNeil, T.F. (1971). Prebirth and postbirth influence on the relationship between creative ability and recorded mental illness. *Journal of Personality, 39,* 391–406.

Miklowitz, D., & Goldstein, M.J. (in press). Mapping the intrafamilial environment of the schizophrenia patient. In R.L. Cromwell & C.R. Snyder (Eds.), *Schizophrenia: Origins, processes, treatment, and outcome*. New York: Oxford University Press.

Sarbin, T.R. (1991). Social construction of schizophrenia. In W.F. Flack, D.R. Miller, & M. Wiener (Eds.), *What is schizophrenia?* (pp. 173–198). New York: Springer Verlag.

Sewell, K.W. (1991). *Conceptual structure of Vietnam combat veterans: Relationship between post-traumatic stress disorder and poorly elaborated trauma constructs*. Unpublished doctoral dissertation, University of Kansas, Lawrence.

Shaw, G.B. (1907). *Major Barbara*. New York: Penguin Books.

Spohn, H.E., & Coyne, L. (1989). *Pathogenic traits in schizophrenia: A proposal for conceptualization, identification, and research utilization*. Unpublished manuscript, Menninger Foundation, Topeka, KS.

Straube, E.R., & Oades, R.D. (1992). *Schizophrenia: Empirical research and findings*. San Diego: Academic Press.

Walker, E.F. (1991). *Schizophrenia: A life-course developmental perspective*. San Diego: Academic Press.

Wang, Z.W., Black, D., Andreasen, N.C., & Crowe, R.R. (1993). A linkage study of Chromosome 11q in schizophrenia. *Archives of General Psychiatry, 50,* 212–216.

This content downloaded from 62.122.79.31 on Sun, 15 Jun 2014 11:42:41 AM
All use subject to JSTOR Terms and Conditions